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PATENT
Attorney Docket No.: 27116-701.301

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:	Confirmation No. 2354
Applicant: Dennis T. Mangano	Group Art Unit: 1614
Serial No.: 09/426,792	Examiner: SPIVACK, P.G.
Filed: October 22, 1999	Customer No. 021971
Title: Methods For Reducing Mortality and Morbidity by Postoperative Administration of a Pharmacologic Cardiovascular Agent	

DECLARATION UNDER 37 C.F.R. §1.132 OF DENNIS T. MANGANO

Mail Stop Amendment
Commissioner For Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Introductory Comments:

This declaration accompanies Applicant's response to the Non-Final Office of October 20, 2004, filed herewith under separate cover.

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I, Dennis T. Mangano, do hereby declare the following:

1. I am the inventor of the invention claimed in the above-identified U.S. patent application.
2. I earned a Bachelors of Science, (B.S.) *summa cum laude* in electrical engineering in 1965, a Masters of Science (M.S.) in electrophysics in 1967 and a Doctor of Philosophy (Ph.D.) in mathematics and physics in 1971 from Polytechnic Institute of Brooklyn, New York. I received a Medical Doctor (M.D.) from the University of Miami, School of Medicine in 1974. My *curriculum vitae* is attached hereto at Exhibit A.
3. My professional training has included an Internship in internal medicine at the University of Miami Medical Center, Miami, Florida from 1974 to 1975 and a Residency in anesthesia at the University of California, San Francisco, California from 1975 to 1977.
4. I have had a Specialty Certification ("board certified") by the American Board of Anesthesiology since 1978.
5. In my professional capacity, I am a professor of Anesthesia and Perioperative Care at the University of California, San Francisco, School of Medicine. I was an Assistant Professor in Residence from 1977-1982, Associate Professor in Residence from 1982 to 1987, Vice-Chairman of the Department of Anesthesia from 1986 to 1995, Professor in Residence from 1987-1990 and Professor of Anesthesia from 1990 to 1998. I have been on a leave of absence from the University of California from August 1998 to the present.
6. I am also a physician at the Veterans Administration Medical Center in San Francisco, California, serving as a Director of Surgical Intensive Care Unit from 1977 to 1990 and as a full time staff physician from 1977 to 2001.
7. I am the founder of the Multicenter Study of Perioperative Ischemia Research Group (McSPI). The McSPI is a consortium of researchers in approximately 150 centers in the United States, Canada and Europe investigating the predictors of myocardial ischemia, infarction, stroke and renal failure in high risk patients undergoing cardiac and non-cardiac surgery.
8. I am the founder and Chief Executive Officer of the Ischemia Research and Education Foundation, a non-profit biomedical research organization that conducts clinical and scientific research specializing in the problems of morbidity and mortality through the study of perioperative ischemia.
9. I have authored and co-authored over 150 scientific papers that have been published in journals such as, *Journal of the American Medical Association*, *New England Journal of Medicine*, *Annals of Cardiac Anesthesia*, *Journal of the American College of Cardiology*,

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Journal of Thoracic and Cardiovascular Surgery, Journal of Cardiothoracic and Vascular Anesthesia and Stroke, among others.

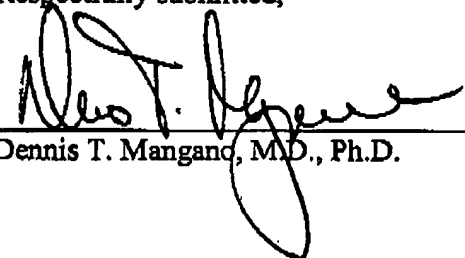
10. I have reviewed the specification of the above-identified patent application (referred to hereinafter as the "specification"), as well as the currently pending claims in the application (referred to hereinafter as the "claims"). I have also reviewed the Non-Final Office Action mailed on October 20, 2004 (referred to hereinafter as the "office action") in connection with the above-identified patent application, and the following references cited therein:
 - a. Goldstein *et al.* 1993, *J. Cardiovasc. Pharmacol.* 22(2): 253-258; and
 - b. Kataria *et al.* 1990, *J. Cardiothoracic Anesth.* 4/5 S2: 13-16
11. Goldstein *et al.* discloses oral administration of atenolol to patients "upon hospitalization on the day before operation" wherein administration is "interrupted 24 h before operation" [see Goldstein *et al.* at page 254, col. 1, paragraph 3]. Goldstein *et al.* further discloses treating patients "2 h after extubation by administration of 1 tablet daily of either 5 mg nebivolol or 50 mg atenolol" and continued daily for 10 days [see Goldstein *et al.* at page 254, col. 2, paragraph 1].
12. In my capacity as an experienced anesthesiologist and cardiologist, I believe that Goldstein *et al.* does not teach or suggest administering the study medication *immediately after surgery* because Goldstein *et al.* discloses administration of said medication after the patient has emerged from anesthesia, and not prior to emergence from anesthesia. I believe that one of ordinary skill in the art, would concur with my understanding of Goldstein *et al.* after reviewing the disclosure as a whole.
13. Kataria *et al.* discloses intravenous infusion of esmolol to patients "during emergence and recovery from anesthesia" [Kataria *et al.* at abstract] following general surgery.
14. In my capacity as an experienced anesthesiologist and cardiologist, I believe that Kataria *et al.* does not teach or suggest administering esmolol *immediately after surgery* because Kataria *et al.* disclose administration of esmolol to patients during emergence from anesthesia, and not prior to emergence from anesthesia. I believe that one of ordinary skill in the art, would concur with my understanding of Kataria *et al.* after reviewing the disclosure as a whole.
15. In summary, neither the reference by Goldstein *et al.* nor the reference by Kataria *et al.* teaches or suggests administering the study medication *immediately after surgery* because these references do not teach or suggest administration of said medication *prior to a patient's emergence from anesthesia* immediately following surgery.

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16. I understand that the phrase "immediately after surgery", as is recited in the specification and claims [see Specification, for example, at page 4, lines 11-18; page 6, lines 1-3; and page 8, lines 18-20], pertains to a specified time when a pharmacologic cardiovascular agent can be administered to a patient, in accordance with an embodiment of my invention. At the time of filing, I understood the phrase "immediately after surgery" in relation to administration of a pharmacologic cardiovascular agent to mean that administration of said agent occurs *prior to a patient's emergence from anesthesia* immediately following surgery.
17. I, the inventor of the invention described and claimed in the above-identified patent application, further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001, and that such willful false statements may jeopardize the validity of the above-identified patent application or any patent issuing thereon.

Respectfully submitted,

By:


Dennis T. Mangano, M.D., Ph.D.

Date:

March 23, 2005